

REMARKS

Upon entry of the above amendments, claims 1, 2, 4-6, 8-10, and 14-19 are pending in this application, among which claims 1, 2, 4, 5, 14, 15, 17, 18, and 19 are pending for further examination on merits, and claims 6, 8-10, and 16 are withdrawn. In this paper, claims 1, 2, 4, 5, 8-10, and 14-16 have been amended, claims 3, 7, and 11-13 have been cancelled, and new claims 17-19 have been added.

Claim 1 has been amended for clarification. Support for the claim amendments can be found throughout Applicants' specification, for example, at lines 9-20 of page 2, lines 22-27 of page 3, lines 1-2 of page 4, Examples 3-6, and 8-11 of the original application.

Claim 2 has been amended in this paper. Support for the claim amendments can be found throughout Applicants' specification, for example, by Examples 3-6, and 8-11.

Claims 4, 5, 8-10 and 16 have been amended for clarification. Support for these amendments can be found in the claims as originally presented. Claims 14 and 15 have been amended in view of the cancellation of claim 7.

Support for the new claim 17 can be found in Applicants' specification at lines 5-6 of page 6 of the as-filed application. Support for the new claim 18 can be found throughout Applicants' specification, for example, at lines 14-15 of page 3. Moreover, support for the new claim 19 can be found throughout Applicants' specification, such as, by Examples 2-11 in the application.

No new matter has been introduced by virtue of the within amendments.

The amendment or cancellation of any claim herein is not to be construed as acquiescence to any of the rejections/objections set forth in the Office Action, and was done solely to expedite prosecution of the application.

Applicants respectfully reserve the right to pursue any non-elected, cancelled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications. Reconsideration of the application is requested in view of the remarks herein.

Co-pending Applications

Applicants wish to take this opportunity to bring into the Examiner's attention that the following U.S. applications are now co-pending before the Office. They are: U.S.

patent application Nos. 10/476,939, 11/885,061, 12/004,933, and 12/569,720. Although all the applications relate to the compound Vardenafil (currently marketed under the trade name: Levitra®), these co-pending applications do not overlap in claimed subject matter with the present application.

Claim Rejections under 35 USC § 112, First Paragraph

Claims 1-5, 7, and 11-15 are rejected under 35 USC § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In particular, the Examiner has asserted that the specification has failed in enabling the “prophylaxis” or “prevention” of the sexual dysfunctions (*see* pages 4 & 5 of the Action). Applicants submit that the rejection against claims 3, 7, and 11-13 are now moot. Applicants respectfully traverse the rejection against the remaining claims.

Without conceding the validity of the rejection and solely for facilitating the prosecution of the present application, the pending claims have been amended in accordance with the Examiner’s suggestion at page 5 of the Action. Applicants point out that the pending method of treatment claims do not recite the “prophylaxis” or “prevention” and that the pending method of production claims have never recited “prophylaxis” or “prevention.” As such, Applicants submit that the subject matter as now claimed is enabled by the disclosure of Applicants’ specification. Therefore, Applicants submit that the instant rejection is now overcome.

Claims 1-5, 7, and 11-15 are also rejected under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Examiner has asserted that the recited process steps have not been presented in such a way as to allow a skilled artisan to know how to carry out the claimed method for producing medicaments (*see* page 6 of the Action). Applicants submit that the rejection against claims 3, 7, and 11-13 are now moot. Applicants further traverse the rejection against the remaining claims.

Nevertheless, without conceding the validity of the rejection and solely for facilitating the prosecution of the present application, claim 1 (together with its dependent claims) has been rewritten to recite specific procedures. Applicants submit that these specific steps as now recited in the pending claims would allow one skilled in

the art to practice the claimed manufacturing process, as the steps are representative of the preparation examples provided in Applicants' specification at pages 10-18. Furthermore, contrary to the Examiner's assertion at page 6 of the Action, the examples in the specification (e.g., Examples 6 and 10) demonstrate that various kinds of excipients may be used in the manufacturing process. As such, Applicants contend that the claimed method of process has been presented in a way that allows one skilled in the art to understand and practice the claimed invention. Accordingly, Applicants submit that the pending claims have satisfied the written description requirement.

Therefore, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, of the pending claims is proper and the same is requested.

Claim Rejections under 35 USC § 103(a)

Claims 1-5, 7, and 11-15 are rejected under 35 USC § 103(a) as allegedly being obvious over Niewohner *et al.* (U.S. Patent No. 6,362,178; hereinafter "Niewohner"). The Examiner states that Niewohner teaches compounds as cGMP-metabolizing phosphodiesterases inhibitors, and their uses for the treatment of sexual dysfunction (page 7 of the Action). The Examiner then asserts that the claimed invention is *prima facie* obvious to one skilled in the art in view of Niewohner's disclosure that its compounds can be present as hydrates (see page 8 of the Action). Applicants submit that the rejection against claims 3, 7, and 11-13 are now moot. Applicants respectfully traverse the rejection against the remaining claims.

To properly determine a *prima facie* case of obviousness, the Examiner "must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made." M.P.E.P. § 2142. This is important as "impermissible hindsight must be avoided and the legal conclusion must be gleaned from the prior art." *Id.* Three criteria may be helpful in determining whether claimed subject matter is obvious under 103(a): first, if there is some suggestion or motivation to modify or combine the cited references; second, if there is a reasonable expectation of success; and third, if the prior art references teach or suggest all the claim limitations. *KSR Int'l Co. v. Teleflex, Inc.* No 04-1350 (U.S. Apr. 30, 2007). With regard to the first criterion, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the

prior art also suggests the desirability of the combination. *In re Mills*, 916 F.3d 690 (Fed. Cir. 1990). “Knowledge in the prior art of every element of a patent claim ... is not of itself sufficient to render claim obvious.” *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1333-34 (Fed. Cir. 2002)]. The issue is whether there is an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *KSR Int'l Co. v. Teleflex, Inc.*

One aspect of the claimed subject matter is directed to a method for producing medicaments in the form of a coated tablet comprising at least one excipient and vardenafil hydrochloride trihydrate (see claim 1). Specifically, the claimed method comprises steps, such as, providing a tablet containing vardenafil hydrochloride with any water content and at least one excipient; treating said tablet with a moistened gas until at least 90 mol% of the vardenafil hydrochloride is converted into the trihydrate form; and coating the tablet. Another aspect of the claimed subject matter is using the coated tablet obtained from the claimed method of production for treating various sexual dysfunctions (see claims 14 and 15).

Although Niewohner mentions that its compounds may be present as hydrates, Niewohner only teaches the preparation of the hydrates through crystallizing a compound from water or a water-containing solvent (see, e.g., lines 22-24 of column 9 in Niewohner; and page 8 of this Action). Applicants note that the reaction conditions disclosed in column 28 of Niewohner do not disclose any specific conditions that could be used for making the hydrates from a pre-formed tablet (as is presently claimed).

Applicants further note that Niewohner does not teach or suggest any step recited in the instantly claimed process method. Indeed, nothing in Niewohner suggests that a moistened gas might be employed in converting any compound into its hydrate form, let alone using a moistened gas in converting vardenafil hydrochloride contained in a pre-formed tablet into its specific hydrate form (i.e., trihydrate). Furthermore, Niewohner does not teach or suggest a process or condition under which a high percentage (e.g., 90% or higher) of the vardenafil hydrochloride may be converted into a single form of the hydrates (that is, trihydrate), rather than being converted into any other forms of the hydrates or a mixture of the hydrates (as discussed in column 9 of Niewohner). Applicants thus contend that Niewohner does not teach any limitations (e.g., steps) of the claimed subject matter.

Applicants further submit that a skilled artisan would not be able to reach the presently claimed subject matter based on the disclosure of Niewohner and/or the common knowledge in the art. It is well appreciated in the art that vardenafil hydrochloride exist in four different polymorphic forms, and that none of these polymorphic forms is preferentially formed at room temperature (see lines 11-19, page 1 of the specification). Moreover, it is known in the art that each polymorphic form of vardenafil hydrochloride takes up different amount of water, depending on the ambient humidity and temperature, and form with water further polymorphic forms called pseudopolymorphs. As a result, the vardenafil hydrochloride hydrates which are the active ingredient of any solid medicaments would exist as a mixture of pseudopolymorphic forms (see lines 27-31, page 1 of the specification). Indeed, following the existing methods in the art, a skilled artisan would have difficulty producing any solid medicaments (such as coated tablets) containing a high percentage of vardenafil hydrochloride in a single form of hydrate (*i.e.*, trihydrate), which is defined and reproducible (see lines 27-30 of page 1 of the specification). In fact, neither Niewohner nor the art teaches or suggests any manufacturing process through which vardenafil hydrochloride contained in a pre-formed tablet will be converted into its single polymorphic form throughout the tablet including the core, let alone a process employing a moistened gas in the step of converting least 90 mol% of vardenafil hydrochloride into its trihydrate form. The ability to convert the hydration state of the core of a pre-formed tablet is not foreseeable from the art.

Still further, Applicants submit that any *prima facie* case of obviousness is rebutted by evidence of the unexpected technical results achieved by the claimed method of production. For instance, Applicants have found that the claimed process is able to produce solid medicaments containing vardenafil hydrochloride trihydrate in a uniform and reproducible form. Applicants also note that the medicaments as produced have negligible changes with respect to the content of water in the crystallization of vardenafil hydrochloride trihydrate. Moreover, the claimed process has unexpectedly achieved a level of 90 mol% or more of the vardenafil hydrochloride in its trihydrate form starting from pre-formed tablets with varying water contents. Applicants respectfully submit that these superior technical results of the claimed process are

clearly unexpected, as neither Niewohner nor the common knowledge in the art ever teaches or suggests these results.

Therefore, Applicants respectfully submit that: first, Niewohner does not teach or suggest each and every element of the present invention; second, nothing in Niewohner nor the common knowledge in the art teaches or suggests a possibility of converting a high percentage of vardenafil hydrochloride contained in a pre-formed tablet, including the core, into its single and reproducible polymorphic form (i.e., trihydrate); and third, based on Niewohner and the common knowledge in the art, there would be no reasonable expectation of success in achieving the unexpected technical results as demonstrated by the present invention. Accordingly, Applicants respectfully submit that the present invention is indeed patentable over Niewohner.

Furthermore, claims 1-5, 7, and 11-15 stand rejected under 35 USC § 103(a) as allegedly being obvious over Niewohner alone or in view of Bischoff *et al.* (WO 01/19357; hereinafter “Bischoff”). Applicants submit that the rejection against claims 3, 7, and 11-13 are now moot. Applicants respectfully traverse the rejection against the remaining claims.

Applicants submit that the afore-mentioned reasoning rebutting the rejection over Niewohner is applicable in addressing the instant rejection, as the present invention is patentable over Niewohner.

Applicants further submit that the addition of Bischoff does not render the subject matter presently claimed obvious. As also noted by the Examiner at page 9 of the Action, Applicants submit that Bischoff only additionally teaches using a cGMP PDE inhibitor in the treatment of sexual dysfunctions, and nothing more. For example, Bischoff does not teach or suggest any method for converting vardenafil hydrochloride contained in a pre-formed tablet, including the core, into any specific hydrate form, let alone a method which provides 90 mol% or more conversion into the single form of trihydrate. Moreover, Bischoff does not teach or suggest any process method employing a moistened gas in the preparation of hydrates. As such, Applicants submit that the combination of Niewohner and Bischoff still does not teach each and every step of the presently claimed process; and thus, the combination of the cited art also does

not teach or suggest the medicaments that would be obtained from the claimed process. Accordingly, Applicants respectfully submit that the present invention is patentable over Niewohner, either alone or in a combination with Bischoff.

Therefore, reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a), of the pending claims is proper and the same is requested.

CONCLUSIONS

In view of the above, each of the presently pending claims in this application is believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicants' undersigned representative to discuss the application. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under the Order No. 83964 (303989).

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Respectfully submitted,

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